

prejudice. Please replace the claims with the clean version provided above. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein. No new matter has been added.

Claims 1-4, 6, 19, 22 and 25 were rejected under 35 USC 112 first paragraph, which rejection was maintained after Applicants' response to the Final Office Action. The Examiner alleges that the specification does not teach what the compound is that is being used to inhibit XRCC4 or how to find it and also that the specification does not disclose the function of XRCC4 and DNA ligase 4.

The present claims are directed at methods of screening for inhibitory compounds. Before performing a screening method, the person skilled in the art does not know the identity of compounds which have inhibitory activity (hence the need for the screening method). Inhibitory compounds are only identified as a result of the method. Any compound may be tested for inhibitory activity using the present methods and these methods are not limited to any particular group or class of compounds. Nor are they limited to compounds which turn out to be inhibitors: using a method of the invention, a particular compound may be found to have no effect whatsoever. Thus, methods of the invention are not limited to any specific compound and there is no need for such limitation in the claims.

Although the choice of compounds which may be screened is unlimited, the person of skill in the art is aware that some classes of compounds are particularly good candidates for possessing inhibitory activity. These classes of compounds are discussed in the specification (for example, on page 15 line 26 to page 16 line 35, page 32 lines 16 to 26 and page 35 lines 34 to page 36 line 3). Thus, while a person skilled in the art may screen any compound he likes using the claimed methods, he is pointed to particularly suitable candidate compounds by the specification. The person skilled in the art is, of course, familiar with the principles and practice of screening methods described in the art (for example, two hybrid assays as described on page 29 line 35 to page 32 line 4).

The specification therefore provides a complete teaching to the person skilled in the art regarding the compounds which might be used in screening methods and how to find them.

The function of XRCC4 and DNA ligase IV is disclosed in sufficient detail in the specification to fully enable the present claims. DNA ligase IV is shown by the present inventors

to be bound to XRCC4 as an active ligase complex within cells. This complex plays a key role in non-homologous end-joining (NHEJ) (i.e. NHEJ does not occur in the absence of the active complex). The function disclosed by the specification therefore represents more than 'mere binding' between XRCC4 and DNA ligase IV: it discloses an active ligase complex which is essential for NHEJ. This disclosure provides fully enables the claimed methods of screening for inhibitors of this complex.

It is noted that the Examiner has proposed claim wording which would overcome her rejection under USC 35 §112 first paragraph. This claim wording has been adopted in the amended claims and the case therefore appears to be in condition for allowance.

Conclusion

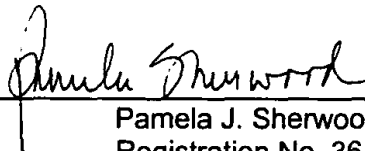
Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number MEWE-005.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 28, 2002

By: _____



Pamela J. Sherwood
Registration No. 36,677

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please cancel claim 2 and 4 without prejudice.

1. [An assay] A method for identifying a compound X which inhibits the binding between XRCC4 (XR-1 Cell Complementing 4) and DNA ligase IV, or XRCC4 and DNA-PK_{CS}/Ku (DNA-dependent Protein Kinase catalytic subunit/Ku) , or XRCC4, DNA ligase IV and DNA-PK_{CS}/Ku, the method comprising the steps of

(i) [bringing into contact] contacting XRCC4 [, a test compound] with compound X and one or more components selected from the group consisting of DNA ligase IV and DNA-PK_{CS}/Ku; under conditions wherein, in the absence of said compound X being an inhibitor of binding, said XRCC4 binds to said one or more components selected from the group consisting of DNA ligase IV and DNA-PK_{CS}/Ku; and

(ii) determining binding between said XRCC4 and said one or more components selected from the group consisting of DNA ligase IV and DNA-PK_{CS}/Ku; reduction or abolition in binding between said XRCC4 and said one or more components selected from the group consisting of DNA ligase IV and DNA-PK_{CS}/Ku being indicative that said compound X inhibits binding between XRCC4 and DNA ligase IV, or XRCC4 and DNA-PK_{CS}/Ku or XRCC4, DNA ligase IV and DNA-PK_{CS}/Ku.

3. (amended) [An assay] A method for identifying a compound X which inhibits DNA ligase IV activity, the method including the steps of:

(i) [bringing into contact] contacting DNA ligase IV, XRCC4 and [a test] compound X; and

(ii) determining DNA ligase activity in the presence and the absence of [test] compound X,

a decrease in the activity in the presence relative to the absence of [test] compound X being indicative that [said test] compound X inhibits the activity of DNA ligase IV

6. (amended) [An assay] A method comprising

(i) [bringing into contact] contacting a [test] compound X, DNA-PK_{CS}/Ku and XRCC4; and

(ii) determining phosphorylation of said XRCC4 in the presence and absence of [test] compound X;

a decrease in phosphorylation in the presence relative to the absence of [test] compound X b ing indicative that [said test] compound X inhibits the phosphorylation of XRCC4 by DNA-PK_{cs}/Ku.

19. (amended) A method comprising obtaining a compound X which inhibits the binding between XRCC4 and DNA ligase IV, or XRCC4 and DNA-PK_{cs}/Ku, or XRCC4 and DNA ligase IV and DNA-PK_{cs}/Ku, employing a method according to claim 1 [or claim 2]; and, formulating said compound X into a composition which comprises a pharmaceutically acceptable excipient.

22. (amended) A method comprising obtaining a compound X which inhibits DNA ligase IV activity employing a method according to claim 3 and formulating said compound X into a composition which comprises a pharmaceutically acceptable excipient.

25. (amended) A method comprising obtaining a compound X which inhibits DNA-PK_{cs}/Ku phosphorylation of XRCC4 employing a method according to claim 6 and formulating said compound X into a composition which comprises a pharmaceutically acceptable excipient.